

REMARKS

This submission is in response to the Official Action dated November 18, 2003. Claims 58, 89, 90, 92, 93, 95, 96 and 98 have been amended. Claim 61 has been canceled, without prejudice or disclaimer. Claims 58, 60, 62-71 and 89-101 are pending. Reconsideration of the above identified application, in view of the amended claims and the following remarks, is respectfully requested.

Claims 58, 89, 90, 92, 93, 95, 96 and 98 have been amended to recite a method comprising administering a composition comprising a biguanide and carrier to the skin and forming a moisture-resistant film on the skin, thereby imparting a persistent antimicrobial activity on the skin. This is supported by the specification, e.g., at page 10, lines 3-12; and by Example 12, pages 32-34.

Claims 58, 90, 93, and 96 have also been amended to incorporate the subject matter of claim 61.

New claim 101 recites that the metallic material is selected from the group consisting of a metal, a metal salt, a metal complex, a metal alloy, and combinations thereof. Support for this claim can be found in the specification, *e.g.* at page 17, lines 26-27.

No new matter has been added by way of this amendment. Each of the Examiner's rejections is discussed below.


REMARKS

Anticipation

The Examiner has maintained the rejection of claims 58, 60-64, and 89-100 as allegedly anticipated under 35 U.S.C. §102(b) by U.S. Patent 4,643,181 to **Brown**. Specifically, the Examiner contends that Brown discloses antimicrobial coating compositions of polycationic polymer such as PHMB which are inherently capable of forming a moisture-resistant film.

This rejection is respectfully traversed. To be anticipatory, a reference must teach each and every aspect of the claimed invention either explicitly or impliedly (MPEP 706.02, emphasis added). The Brown patent does not disclose antimicrobial compositions comprising a biguanide polymer and a metallic material. For this reason alone, this reference fails to anticipate the claimed invention.

Further, as amended, the claims all recite, directly or by dependency, a two step method for providing antimicrobial activity comprising (i) applying compositions to the skin and (ii) forming a moisture-resistant film on the skin, thereby imparting persistent antimicrobial activity on the skin. The Brown patent neither discloses nor suggests such a method. Instead, Brown's composition is contained in a surgical dressing, and is "activated" by the moisture from a patient's skin (Brown, column 4, lines 40-44). There is nothing in the Brown patent to suggest direct application to skin to form a film on the skin, much less a moisture-resistant film, or even a suggestion that such an application might be desirable.

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Accordingly, since the compositions of Brown do not contain a metallic material, are not moisture resistant, and are not administered directly to the skin or form a film thereon, but are instead comprised in a dressing adhered to the patient, the method of each of claims 58, 90, 92 93, 95, 96, and 98, and claims dependent thereon, is novel and unobvious over this reference.

The Examiner has rejected claims 58, 60-71 and 89-100 as allegedly anticipated under 35 U.S.C. §102(e) by Larkin et al. (Ophthalmology 1992:99:185-191). Specifically, the Examiner contends that Larkin et al. describes topical compositions comprising PHMB for treating infections in patients. Upon entry of the present amendment, all claims recite a metallic material. Similar to the Brown patent, the Larkin reference does not teach or suggest an antimicrobial composition comprising a metallic material. Thus, this reference cannot anticipate the claimed invention.

Moreover, Larkin discloses treatment of patients with keratitis, i.e. , inflammation of the cornea of the eye, with 0.02% PHMB solution (page 186). Larkin does not describe or suggest the PHMB solution is applied to the skin of patients. Instead, to treat the keratitis, the PHMB solution is directly administered to the cornea (via eye-drops, etc.). Since the cornea is always wet from tear liquid, the PHMB stays in solution, *i.e.* it is not made to form a film, nor intended to form a film. Furthermore, the formation of any moisture-resistant film on the cornea

would disrupt the physiological function of corneal epithelium and therefore be highly undesirable. The formation of a moisture-resistant film on the cornea would be detrimental to the health of a patient's eye and hence would be contrary to the intended function of the Larkin composition.

Since the Larkin publication fails to teach or suggest any compositions comprising a metallic material, any administration to skin, or even forming a persistent moisture-resistant antimicrobial film on skin, and also teaches away from the formation of a moisture-resistant film, the instant claims are novel and unobvious over this reference.

The Examiner has maintained the rejection of claims 58, 60-71, and 89-100 as allegedly anticipated under 35 U.S.C. §102(b) U.S. Patent 5,817,325 to **Sawan et al.** (filed October 28, 1996). Specifically, the Examiner contends that Sawan et al. discloses methods and compositions comprising PHMB/MBDGA-silver coating on a device or dermal composition.

As discussed in previous Response dated February 12, 2004, Sawan et al. describes antimicrobial compositions which can be formed by casting a free-standing film, grinding the film to a *powder*, then incorporating the *powder* into a carrier such as a gel, cream, or liquid. The carrier can be used "as a topical antiseptic and be applied to a wound" (Sawan et al., col. 5, l. 64 to col. 6, l. 2). However, as amended the claims do not recite powder compositions. Furthermore,

how any powder dispersion could form a film on the wound, much less on intact skin, is not described in the reference, nor is any such mechanisms proposed by the Examiner. For example, assume that the powder would behave like a substance such as talcum powder. If a formulation containing talcum powder is applied to the skin in a vehicle, the skilled artisan would not expect the powder to form a continuous film. Rather, after drying, the dried composition would remain as individual powder particles that could readily be brushed away. There are no molecular reasons for powder particles to adhere to one another and form a film, as they are individual particles that do not undergo any transition or substantial interaction to achieve assembly into a film structure. Accordingly, there is no teaching, explicit or inherent, in Sawan et al. that the powder particles described would have any ability to form a moisture-resistant film on skin.

Thus, the Sawan et al. patent does not teach or suggest any topical antiseptics that would form an antimicrobial film when applied to the skin. Accordingly, this reference does not anticipate or render obvious the claimed invention set forth by the amended claims.

For the above reasons, reconsideration and withdrawal of all of the Examiners rejections under 35 U.S.C. §102 is respectfully requested.

Double-Patenting

All claims have been rejected by the Examiner under the judicially created doctrine of obviousness-type double-patenting as being allegedly unpatentable over various claims in commonly-owned U.S. Patents 6,180,584; 6,030,632; 5,869,072; and 5,817,325.

Upon indication of allowable subject matter in the present application, the allowable subject matter not being patentably distinct from the claims of one or more of the above-cited patents, an appropriate terminal disclaimer will be timely filed.

Obviousness

The Examiner has maintained the rejection of claims 58, 60-71 and 89-100 as allegedly obvious over **Brown** in view of **Sawan** et al. WO 95/17152 ('152). The Examiner acknowledges that Brown fails to teach the linking of PHMB biguanide polymers to a water-insoluble organic compound, but asserts that the '152 publication provides this teaching, and contends that it would have been obvious to crosslink Brown's PHMB with the MBDGA of the '152 publication to enhance the therapeutic effects.

As discussed above under the section entitled "Anticipation," neither the Brown patent nor the Sawan et al. publication in any way teaches or suggests a two step method of (i) administering an antimicrobial composition and (ii) forming

a moisture-resistant antimicrobial barrier or film on the skin. The '152 publication is clearly concerned with coated articles for holding preservative-free liquids, and does not describe any applications resulting in a film being formed on the skin. The Brown patent describes substrates (i.e., fabrics or polymer films of polyurethane or copolyester) having "high moisture vapor transmission rates" (Brown, column 2, lines 22-49) whereas the method of the claimed invention provides for administering topical compositions and forming a moisture-resistant film on the skin. Accordingly, Brown teaches away from forming any moisture resistant film, whether applied on an article or to skin.

However, even when forcibly combined, the combined teachings of the Brown patent and '152 publication fail to render the claimed invention obvious since neither reference discloses the administration of topical compositions, or the formation of a moisture-resistant film on the skin. As set forth by the MPEP, section 2142, "[t]he prior art reference (or references when combined) must teach or suggest all the claim limitations." Thus, despite the Examiner's allegations that the references were not "considered as a whole", when a teaching is missing from both references, the combination cannot make up for this flaw. The claims listed in the present submission are therefore unobvious over the combination of Brown and the '152 publication, and reconsideration and withdrawal of this rejection is therefore respectfully requested.

All claims have been rejected as allegedly obvious over **Lowry et al.** U.S. Patent 6,509,022. The Examiner contends that Lowry discloses polymeric biguanide compositions for topical delivery.

Contrary to what is suggested in the present Office Action, Lowry does not teach a method as defined by the claims of the present invention. Unlike the above amended claims, the Lowry does not specifically teach polymer biguanide compositions for topical delivery comprising a *metallic material*. As emphasized above, the prior art reference must teach or suggest all the claim limitations. The Lowry Patent therefore cannot render obvious claims calling for compositions comprising a metallic material. Accordingly, Applicant respectfully requests withdrawal of this rejection.

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Therefore, in view of the above amendments and remarks, it is earnestly requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,



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Limited Recognition Under 37 C.F.R.
§10.9(b) (see attached)
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